Atty. Dkt. No. 068390-0102

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Mitsuo NISHIKAWA

Title: POLYPEPTIDE HAVING AN ACTIVITY TO SUPPORT PROLIFERATION OR SURVIVAL OF HEMATOPOIETIC STEM CELL OR HEMATOPOIETIC PROGENITOR CELL, AND DNA CODING FOR THE SAME

Appl. No.: 10/512,109

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Examiner: Bridget E. Bunner

Art Unit: 1647

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DECLARATION UNDER 37 C.F.R. § 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Mitsuo Nishikawa, declare the following:

1. I am the named inventor in the captioned application.

2. I understand that claims 6-8 and 13 of the application are rejected in view of a patent document, U.S. Publication No. 2003/0022217, which published in the name of Ceccardi *et al*. I also understand that this Ceccardi publication is asserted to have an art-effective date of July 2, 2001.

3. I conceived the inventions claimed in the captioned application before July 2, 2001. In this regard, I submit as Exhibits A & B copies of U.S. Provisional Application No. 60/297,286 ("the '286 application) filed on June 11, 2001 in Japanese and English,

respectively. I also enclose as Exhibit C relevant portions of a laboratory notebook of Dr. Minoru Kakeda, a researcher who worked in my laboratory under my direction and supervision.

4. The '286 application shows possession of the nucleotide and amino acid sequences of mouse SCR-6, the murine homolog of the polypeptide recited in the pending claims. *See, e.g.* English version of U.S. Provisional Application No. 60/297,286, pg. 73, ln. 4-9. As noted in the present application, I first isolated and sequenced murine SCR-6 and then, using sequence information obtained therefrom, turned to the human protein. *See* US 2005/0255546, ¶¶ 215 to 219.

5. Pages 59 and 60 of Dr. Kakeda's notebook, which are dated June 25 to June 26, 2001, show cycle sequencing reactions performed on an isolated, human DNA fragment encoding human SCR-6.

6. Thus, the cited passages show that before July 2, 2001, I had conceived of a human SCR-6 polypeptide as recited in claims 6-8 and 13.

7. The compositions claimed in the captioned application were reduced to practice on July 6, 2001. In this regard, pages 59 and 60 of Dr. Kakeda's notebook show that cycle sequencing reactions were performed on an isolated, human DNA fragment encoding human SCR-6 on June 25 and June 26, 2001. Pages 61-63 of Dr. Kakeda's notebook, dated July 6, 2001, show the elucidated nucleic and amino acid sequences of the isolated human SCR-6 polypeptide. Thus, the cited pages demonstrate that I possessed an isolated human SCR-6 polypeptide (*i.e.*,. SEQ ID NO: 48), as well its encoding DNA (*i.e.*, SEQ ID NO: 47) as of July 7, 2001.

8. I understand that I also must show diligence in the completion of the invention from a time just prior to the date of the Ceccardi reference up to the date of my actual reduction to practice, which I understand to be July 6, 2001. As noted above, pages 59 and 60 of Dr. Kakeda's notebook show that cycle sequencing reactions were performed on an isolated, human DNA fragment encoding human SCR-6 on June 25 and June 26, 2001. The ensuing amplicons were run on an ABI377 DNA sequencer, and the results analyzed. Pages

61-63 of Dr. Kakeda's notebook, dated July 6, 2001, show the elucidated nucleic and amino acid sequences of the isolated human SCR-6 polypeptide.

9. A person knowledgeable in the field of molecular biology, *circa* June-July of 2001, readily would have recognized from the above-discussed materials that, as of July 6, 2001, I possessed an isolated polypeptide that is an expression product of the DNA of SEQ ID NO: 47 and that has an activity to support proliferation of erythroid progenitor cells, as stated in claims 6 and 7 of the captioned application. Such a person would have considered a composition as claimed in the application to be, I believe, a routine and reasonably predictable next step from the June-July 2001 experiment described above. That is, with (i) the nucleic acid sequence of human SCR-6 (SEQ ID NO: 47), (ii) working amplification primers, and (iii) an isolated DNA fragment in hand, a practitioner in molecular biology readily could have made an expression construct to produce recombinant human SCR-6. Furthermore, because human SCR-6 shares more than 95% homology with murine SCR-6 (*See* Dr. Kakeda's notebook, page 61, and US 2005/0255546, ¶ 219), the practitioner reasonably would have expected human SCR-6 to possess a similar functionality as its murine homolog, which functionality was demonstrated in Example 6 of the '286 application.

10. In addition, a person knowledgeable in the field of molecular biology, *circa* June-July of 2001, readily would have recognized from the above-discussed materials that, as of July 6, 2001, I possessed an isolated polypeptide that is an expression product of the DNA of SEQ ID NO: 47, has an activity to support proliferation of erythroid progenitor cells, and is modified with one or more modifying agents selected from the group consisting of polyethylene glycol (PEG), dextran, poly(N-vinyl-pyrrolidone), polypropylene glycol homopolymer, copolymer of polypropylene oxide/ethylene oxide, polyoxyethylated polyol, and polyvinyl alcohol, as stated in claim 8. A person familiar with the biologics field would have considered such a modification obvious in view of the above-cited passages, since such modifications were widely used in the field, *circa* June-July of 2001, to stabilize therapeutic proteins in vivo and increase their half-life. *See, e.g.*, Bailon et al., "Polyethylene glycol-conjugated pharmaceutical proteins," *Pharmaceutical Science & Technology Today*, 1: 352-56 (1998), provided here as Exhibit D.

11. Similarly, a person knowledgeable in the field of molecular biology, *circa* June-July of 2001, readily would have recognized from the above-discussed materials that, as of July 6, 2001, I possessed a composition having an effect to support proliferation of erythroid progenitor cells, which composition comprises an effective amount of a human SCR-6 polypeptide, as stated in claim 13. In particular, a person familiar with the biologics field would have considered such a composition obvious in view of the June-July 2001 experiment, described above, and the '286 application. Thus, such a person would have appreciated that a practical use of a recombinant human SCR-6 protein, as elucidated by the June-July 2001 experiment, would be to stimulate proliferation of erythroid progenitor cells. Moreover, in light of the success exemplified in the '286 application with the highly homologous murine SCR-6, this person artisan would have had a reasonable basis of expecting success in formulating such a composition.

12. I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

May 1, 2008
Date

Mitsuo Nishikawa